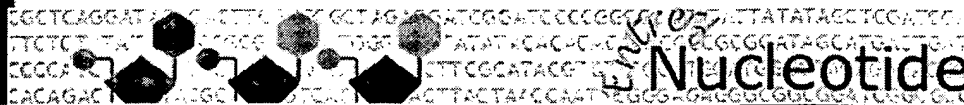


U.S. Serial No. 10/650,108  
Amendment Dated 03/16/2005  
Reply to Office Action of 12/16/2004



## APPENDIX

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for mre11

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Details

Field: Gene Name, Limits: Publication Date from 1900/01/01 to 2000/04/18

Display

Summary

Show: 20

Send to

Text

All: 11

bacteria: 0

mRNA: 5

RefSeq: 3



Items 1 - 11 of 11

One page.

☐ 1:

Reports

Links

NM\_005590

Homo sapiens MRE11 meiotic recombination 11 homolog A (S. cerevisiae) (MRE11A), transcript variant 2, mRNA  
gi|56550106|ref|NM\_005590.3|[56550106]

☐ 2:

Reports

Links

NM\_005591

Homo sapiens MRE11 meiotic recombination 11 homolog A (S. cerevisiae) (MRE11A), transcript variant 1, mRNA  
gi|56550105|ref|NM\_005591.3|[56550105]

☐ 3:

Reports

Links

NC\_001145

Saccharomyces cerevisiae chromosome XIII, complete chromosome sequence  
gi|44829554|ref|NC\_001145.2|[44829554]

☐ 4:AE003631 Reports

Links

Drosophila melanogaster chromosome 2L, section 40 of 83 of the complete sequence  
gi|55380441|gb|AE003631.4|[55380441]

☐ 5:D11463 Reports

Links

S. cerevisiae MRE11 gene for Mre11 protein, complete cds  
gi|1513064|dbj|D11463.1|YSCMRE11[1513064]

☐ 6:AJ243822 Reports

Links

Arabidopsis thaliana mRNA for Mre11 protein (MRE11 gene)  
gi|5524768|emb|AJ243822.1|ATH243822[5524768]

☐ 7:AF178433 Reports

Links

Coprinus cinereus DNA repair and meiosis protein Mre11 (mre11) gene, complete cds  
gi|5916239|gb|AF178433.1|AF178433[5916239]

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Related resources  
BLASTReference sequence  
project

Search for Genes

Submit to GenBank

Search for full length  
cDNAs

- ☐ **8:** [AF132144](#) Reports Links  
Drosophila melanogaster clone LD08638 endo/exonuclease Mre11 (mre11) mRNA,  
complete cds  
gi|4928449|gb|AF132144.1|AF132144[4928449]
- ☐ **9:** [AF134569](#) Reports Links  
Xenopus laevis putative nuclease Mre11 (MRE11) mRNA, complete cds  
gi|4884903|gb|AF134569.1|AF134569[4884903]
- ☐ **10:** [Z49939](#) Reports Links  
S.cerevisiae chromosome XIII cosmid 9959  
gi|887599|emb|Z49939.1|SC9959[887599]
- ☐ **11:** [U60829](#) Reports Links  
Saccharomyces cerevisiae Mre11p (MRE11) gene, complete cds  
gi|2209264|gb|U60829.1|SCU60829[2209264]

Display	Summary	Show: 20	Send to	Text
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					<a href="#">Help</a>
Analysis Browser:					<a href="#">Level Up</a>

Report for **1264\_Mre11\_sid2 (Protein)** [Update](#)

Description Case 1264 Mre11 sid2 [Edit](#)

Function **Double-strand break repair protein MRE11.**

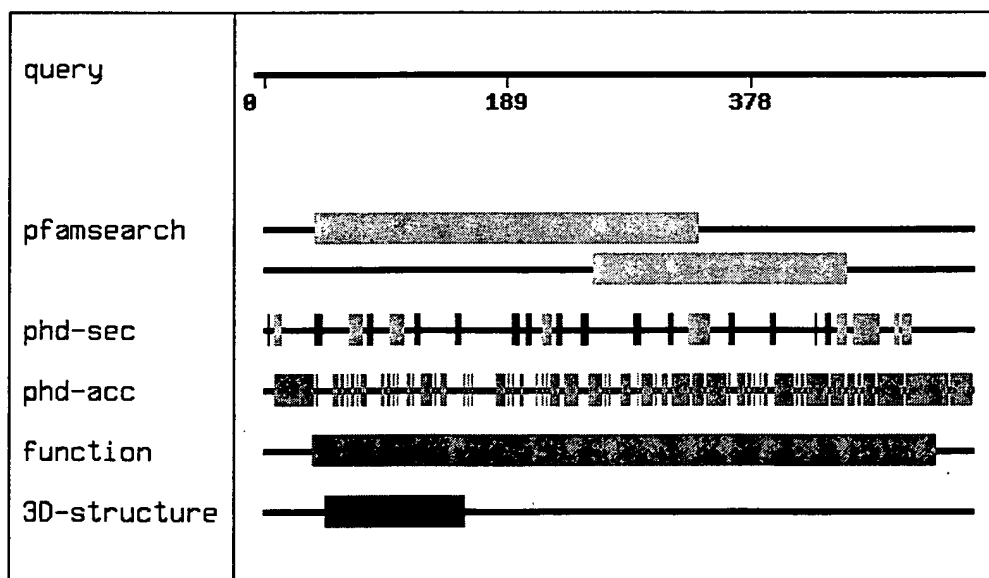
**Direct assignment of functionality by identity to**  
[swissnew|Q9XGM2|MR11\\_ARATH](#)

in region **39** to **523** for overall length of **720** (87% of query, 67% of hit, [see the alignment](#) ).

**Functional class** Replication

**Extracted keywords** [Nuclease](#), [Endonuclease](#), [DNA repair](#), [Meiosis](#),  
[Hydrolase](#), [Nuclear protein](#), [Exonuclease](#), [Manganese](#)

#### Features Summary



#### Homologies

		<a href="#">All BLAST hits</a>
<b>Protein</b>	<b>41 clear homologs</b>	<a href="#">All protein BLAST hits</a>
<b>ESTs</b>	<b>115 homologs</b>	<a href="#">All EST BLAST hits</a>
<b>Patents</b>	<b>37 homologs</b>	<a href="#">All patent hits</a>

Appendix  
Part 2

Pramod B. Mahajan  
Serial No. 10/650,108

## General

### Gene name

**Molecular weight** 61.86 kD

**Sequence length** 552

**Isoelectric point** 5.64

**Predicted cellular localisation (PHD and PreLoc)** nuclear (50.5 %)

**Identical sequence segments in:** trembl|AX287091|AX287091\_1  
gp|AX287091|17049072

## 3D Structure

**3D structure inferred by clear homology from residues 48 to 157 in 1II7-A**

**View** alignment

pdb|1II7|1II7-A structure

## Phylogeny

**Distribution** 28 species extracted from 133 Species  
homologous sequences.

**Taxa** Chordata, Eukaryotae, Fungi,  
Planta

**Model organisms** *Arabidopsis thaliana*,  
*Caenorhabditis elegans*,  
*Drosophila melanogaster*,  
*Homo sapiens*, *Mus musculus*,  
*Saccharomyces cerevisiae*

## Features

**No significant hits detected by** [Coils] [Phd-tm] [seg] biasdb

## Patterns

**Mre11 DNA-binding presumed domain region** from residue **258** to **453**. Source: [pfamsearch] .  
Quality: (E=1.9e-85)

**Calcineurin-like phosphoesterase region** from residue **41** to **338**. Source: [pfamsearch] . Quality:  
(E=2.3e-09)

**No significant hits found in** [prosiste database] [blocks database]

## Comment

No comment section.

[Edit](#)

## Completed Tasks

**Start Time**

**User**

**Comment**

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[Interactiv](#)

07.03.2003, dressvm  
14:04:36

bioSCOUT\_default [details...](#)

1

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---

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Alignment: 1264\_Mre11\_sid2 - pdb|1II7|1II7-A

---

## BLASTP - alignment of 1264\_Mre11\_sid2 against pdb|1II7|1II7-A

mre11 nuclease

- This hit is scoring at : 3e-06 (expectation value)
- Alignment length (overlap) : 111
- Identities : 32 %
- Scoring matrix : BLOSUM62 (used to infer consensus pattern)
- Database searched : nrdb

```

Q:      48 DCHLGMEKDEIRRFDSF-QAFEEICALADKNKVDFILLGGDLFHENKPSRSTLVKTIEI
      D.HLGY : . : :R :.F :AF:.....A :..VDFIL:.GDLFH.:PS .TL K.I.:
H:      8 DIHLGYEQFHKPQREEEFAEAFKNALEIAVQENVDFILIAGDLFHSSRPSPGTLKKAIAL

      LRRYCLNDQPVKFQVSDQTVNFPNRFQVNYEDPNFNVGLPVFTIHGNHD      157
      L          Q: :.:.:          PVF.I.GNHD
      L-----QIPKEHSI-----PVFAIEGNHD      86
    
```

---

### Legend of Alignment

- : positive score
  - . score between -2 and 0
- 

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HEADER REPLICATION 20-APR-01 1II7  
TITLE CRYSTAL STRUCTURE OF P. FURIOSUS MRE11 WITH MANGANESE AND  
TITLE 2 DAMP  
COMPND MOL\_ID: 1;  
COMPND 2 MOLECULE: MRE11 NUCLEASE;  
COMPND 3 CHAIN: A, B;  
COMPND 4 ENGINEERED: YES  
SOURCE MOL\_ID: 1;  
SOURCE 2 ORGANISM\_SCIENTIFIC: PYROCOCCUS FURIOSUS;  
SOURCE 3 ORGANISM\_COMMON: ARCHAEA;  
SOURCE 4 EXPRESSION\_SYSTEM: ESCHERICHIA COLI;  
SOURCE 5 EXPRESSION\_SYSTEM\_COMMON: BACTERIA  
KEYWDS RAD50, MRE11, DNA DOUBLE-STRAND BREAK REPAIR, DAMP,  
KEYWDS 2 MANGANESE  
EXPDTA X-RAY DIFFRACTION  
AUTHOR K.-P.HOPFNER,A.KARCHER,L.CRAIG,T.T.WOO,J.P.CARNEY,J.A.TAINER  
REVDAT 1 30-MAY-01 1II7 0  
JRNL AUTH K.-P.HOPFNER,A.KARCHER,L.CRAIG,T.T.WOO,J.P.CARNEY,  
JRNL AUTH 2 J.A.TAINER  
JRNL TITL STRUCTURAL BIOCHEMISTRY AND INTERACTION  
JRNL TITL 2 ARCHITECTURE OF THE DNA DOUBLE-STRAND BREAK REPAIR  
JRNL TITL 3 MRE11 NUCLEASE AND RAD50 ATPASE  
JRNL REF CELL (CAMBRIDGE,MASS.) V. 105 473 2001  
JRNL REFN ASTM CELLB5 US ISSN 0092-8674





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				Help	Features

## Summary

Searched query 1264\_Mre11\_sid2 against PFAM database.

Hit	Score	Expect	Description	Q from	Q to	Method
<input type="checkbox"/> <a href="#">pfam hmm Mre11_DNA_bind. alignment</a>	297.3	1.9e-85	Mre11 DNA-binding presumed domain	258	453	HMMPFAM
<input type="checkbox"/> <a href="#">pfam hmm Metallophos. alignment</a>	44.6	2.3e-09	Calcineurin-like phosphoesterase	41	338	HMMPFAM

<a href="#">New Task</a>	<a href="#">Rename Sequences</a>
--------------------------	----------------------------------

Please report problems and feedback concerning bioSCOUT through the [support interface](#).



Alignment: 1264\_Mre11\_sid2 - pfam|hmm|Mre11\_DNA\_bind

## HMMPFAM - alignment of 1264\_Mre11\_sid2 against pfam|hmm|Mre11\_DNA\_bind

Mre11 DNA-binding presumed domain

- This hit is scoring at : 297.3
- Scoring matrix : BLOSUM62 (used to infer consensus pattern)

```

Q: 258 KTNPKSAINEHFL---PGSSVATSLIDGEAKPKHVLLLEIK-GNQYRPTKIPLRSVRPFE
   .:P:. .: F. PGSSVATSL .GEA PKHV LLEIK G.:. T.IPL::VRPF
H: 1 lIdPeenegkgFyVtQPGSSVATSLspGEAlpKHVgLLeIkYGkkFkltpIPLqTVRPFv

YAEVVLKDEADV----NSNDQDS--VLEHLDK-IVRNLIKSSQ-----PTA-SRS
..E:VL.DE.D: ..ND.D. : :.L : V.:I:..... . . .
mkeiVLadepdilglDrpndtdeRYIqkfLieAkVeemIdeAnaewkekqAdvklgDepr

EPKLPLVRIKVDYSG-----FSTINPQRFQKYVGKVANPQDILIFSKSAKKRQTG
:P.LPL:R::VDY:G :.T.NP RFGQ::VG:VANP.D:: F.K..K:.....
qPpLPLIRLrVDYtggn tqdwldyqt fNpiRFgqrFvGrVANpnDvvqFkkkkKpkekka

D-----HIDDSEKL RPEELNQQTIEALV-----AESNLKMEILPVDDLDIALHD
: . D.E L..E:LN. :.E.LV AE.N :.:LP .L. A:..
nteveiNftkllddrdeellaseklaln rVetLVneYletAeknkqLslLperglgeAvqe

F 453
F
F 241
    
```

### Legend of Alignment

- : positive score
- . score between -2 and 0

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Projects	Analyses	Admin	Alert	SRS	Tutorial
				Help	Features

Alignment: 1264\_Mre11\_sid2 - pfam|hmm|Metallophos

---

## HMMPFAM - alignment of 1264\_Mre11\_sid2 against pfam|hmm|Metallophos

Calcineurin-like phosphoesterase

- This hit is scoring at : 44.6
- Scoring matrix : BLOSUM62 (used to infer consensus pattern)

```

Q:      41 LRILVATDCHLGYPEKdeirrfdsfqafEEICALAdKnKVDFILLGGDLFHENKPSRSTL
      :RILV. D.H G: :                               :..LA : K D.:L. GDL.....PS ..L
H:      1 mrilvigDlHggfedl.....l1lllela.e.kpdlvlf1GDldvrgppslevl

      VKTieilrryclndqpvkfqvvsdqtvnfpnrfgkvnyEDPNFNVGLPVFTIHGNHDDPA
      :.                               .... PV:...GNHD ..
      l1l.....falklkapgpvylvrGNHDfds

      GVDNLsaidilsacnlvnyfgkmdlgsgvgqiavypvlvkkgmtsvalyglgnirderl
      G . .
      gnsvy.....

      nrmfqtphSVQWMRPGtQDGESaSDWFN1LVHQNRIKTnpksaine hflpgssvatsli
      :... : .IL::H . ..
      .....welfleef.l1lla.lvdgkillvHgglspd.....

      dgeakpkhvl1leikgnqyrptkiplrsvrpfeyaevvlkDEADVNsNDQDSVL---EH1
      E. :. N. D V: .H
      .....leellk.ngvdlvirGHtH.

D      338
.
p      124
    
```

---

### Legend of Alignment

- : positive score
  - . score between -2 and 0
- 

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```
!!AA_MULTIPLE_ALIGNMENT 1.0
FileUp of: @/tmp/47563335.list
```

Symbol comparison table: genrundata:blosum62.cmp    CompCheck: 1102

GapWeight: 8      GapLengthWeight: 2

```
1264AB010695_pileup_47563.txt  MSF: 805  Type: P  March 13, 2003 16:53  Check:
7228 ..
```

U37359aa	Human Mre11 protein encoded by GenBank U37359
U58987aa	Mouse Mre11 protein encoded by GenBank U58987
AB010695aa	Arabidopsis Mre11 protein encoded by GenBank AB010695
AJ243822aa	Arabidopsis Mre11 protein encoded by GenBank AJ243822
<b>1264sid2</b>	<b>Case 1264 Mre11 SEQ ID NO: 2</b>
D11463aa	<i>S. cerevisiae</i> Mre11 protein encoded by GenBank D11463
X82322	<i>S. pombe</i> Rad32 protein encoded by GenBank X82322

Identical to 1264s162

\* Conserved Asp required for nuclease activity (Example 4)

Underlined phosphodiesterase/nuclease motifs (Example 4)

Double-underlined Pfam MRE11 DNA bind domain (Quality E=1.9e-85)

Italicized Pfam Metallophos domain (Quality E=2.3e-09)

	1	50
AB010695aa	~~~~~ ~~~~ MSREDFSDI LR LVATDCH	
AJ243822aa	~~~~~ ~~~~ MSREDFSDI LR LVATDCH	
<b>1264sid2</b>	MVGFC <del>SALDL</del> QQRIGLANTL SSGSMS <del>EPEQ</del> PGGGEGVNT LRLVL <del>VLCGH</del>	* Asp
U37359aa	~~~~~ ~~~~ MS T DALDDENI F ILIVATDIH	Pfam_metal
U58987aa	~~~~~ ~~~~ MS E DPLDDEDI F ILIVATDIH	
D11463aa	~~~~~ ~~~~ MDYPDPDI RRI TCNH	
X82322aa	~~~~~ ~~~~ MPN ED MNNELHNENT RRL DPH	

51 100  
 AB010695aa LGYMEKDEIR RHDSEKAPEE IC A EKQV DI LIGCDLF HENKPSR T1  
 AJ243822aa LGYMEKDEIR RHDSEKAPEE IC A EKQV DI LIGCDLF HENKPSR T1  
 1264sid2 LGYMEKDEIR RHDSEKAPEE IC A EKQV DI LIGCDLF HENKPSR T1 Motif  
 U37359aa LG MEKDAAR GNDIFV L E ILRLAQENEV DFTLLCGDLF HENKPSRKTL  
 U58987aa LG MEKDA R GNDIFV F E ILRLALENEV DFTLLCGDLF HENKPSRKTL  
 D11463aa GYNENPIT GDDS K L EHE MMLAKNNNV DM QSCDLF HVNKPS K L  
 X82322aa GYGEKDP R GNDSEV LNE HLE ARERDV DM LIGCD F H NKPSRK L

101 150

AB010695aa VK IETLRRH CLNDKPVQEQ VVSDQTVNEQ .NATGQVNYE DPHENVGLPV

AJ243822aa VK IETLRRH CLNDKPVQEQ VVSDQTVNEQ .NATGQVNYE DPHENVGLPV

**1264sid2** VK IETLRRH CLNDKPVQEQ VVSDQTVNEQ .NATGQVNYE DPHENVGLPV

U37359aa HTC E L R Y C GDRPVQFE SDQ VNEG FS EPWVNYQ DGNLN S PV

U58987aa HSC E L R Y C GDRPVQFE V SDQ VNEG FS EPWVNYQ DGNLN S PV

D11463aa YQV KTLRLC C GDKPECELE SDP QVEH YDEFTNVNYE DPNFN S PV

X82322aa YQ RSLRLN CLGDKPECELE SDT TTG DTAVCN NYL DPNINVA EV

	151		200	
AB010695aa	E I HGNHDDP AGVDNL SAID ILSACNLVNY FGK MVLGGSG VGOI YPVL			
AJ243822aa	E I HGNHDDP AGVDNL SAID ILSACNLVNY FGK MVLGGSG VGOI YPVL			
1264sid2	<b>E I HGNHDDP AGVDNL SAID ILSACNLVNY FGK MVLGGSG VGOI YPVL</b>			<b>Motif</b>
U37359aa	E I HGNHDDP GADALCA D ILSACG FVNH EG SM....S MEKID SPVL			
U58987aa	E I HGNHDDP GADALCA D ILSACG FVNH EG SM....S MEKID SPVL			
D11463aa	EGLSGNHDDA GDSL LCP D L L HATGL NH EGK I....E SDKIKVVP L			
X82322aa	E I HGNHDDP GDGRYSA D L L QVTGLVNY EG P....E ND IIVVSP L			

	201		250
AB010695aa	KKGST VAL YGLGNIRDER LNRMFOTPH VQWMRHEVO GCDVSDWFNT		
AJ243822aa	KKGST VAL YGLGNIRDER LNRMFOTPH VQWMRHEVO GCDVSDWFNT		
1264sid2	<b>KKGST VAL YGLGNIRDER LNRMFOTPH VQWMRHEVO GCDVSDWFNT</b>		
U37359aa	QKGSTK AL YGLGSIPDER IYRMFVN.KK VTM RHKED N....SWFN		
U58987aa	QKGSTK AL YGLGSIPDER IYRMFVN.KK VTM RHKED N....SWFN		
D11463aa	FQKGSTK AL YGLAA RDER LFRTEKD.GG VTFEVETMR G....SWFN		
X82322aa	QKGSTK AL YG SN RDER LYHSERE.NK VK REDLYR D....SWFN		

	251		300
AB010695aa	LVLHQNR K NPKNAISEHF LPRFLDFIVW GHEHECLIDP QEVSGMGFHI		
AJ243822aa	LVLHQNR K NPKNAISEHF LPRFLDFIVW GHEHECLIDP QEVSGMGFHI		
1264sid2	<b>LVLHQNR K NPKNAISEHF LPRFLDFIVW GHEHECLIDP QEVSGMGFHI</b>		
U37359aa	FV LHQNRSKH GSTNFIPEQF LDDFIDLVIW GHEHECKIAP TKNEQQLFYI		
U58987aa	FV LHQNRSKH GNTNFIPEQF LDDFIDLVIW GHEHECKIGP IKNEQQLFYI		
D11463aa	LC HQNHTGH TNT F PEQF LPDFLDMVIW GHEHECIPNL VHNPIKNFDV		
X82322aa	LT HQNHSAH TETSYP ESE QDFYDFVLW GHEHECLIDG SYNPTQKFTV		

	301		350	
AB010695aa	TQPGSSVATS LIDGES KPKH VLLLEIK.GN QYRPTKIPI T SVRPFEEYE			
AJ243822aa	TQPGSSVATS LIDGES KPKH VLLLEIK.GN QYRPTKIPI T SVRPFEEYE			
1264sid2	<b>..PGSSVATS LIDGEAKPKH VLLLEIK.GN QYRPTKIPI LR SVRPFEEYE</b>			<b>Mre11_DNA</b>
U37359aa	SQPGSSVATS LSPGEAVKKH VGLLRIK.GR KMNMHKIP L VRQFME			
U58987aa	SQPGSSVATS LSPGEAVKKH VGLLRIK.GR KMNMOK PLR VRREFIE V			
D11463aa	LQPGSSVATS LC AEAQPKY MFL LKYCE AP MFIPIE RTEKMKS			
X82322aa	VQPGS ATS LSPGEAPKH CG LINTT.GK D HLEKIRLR VRPFIMK			

	351		400
AB010695aa	VLKDE D DP NDQNS .... LEHLDK VRN..... LIEK SKK		
AJ243822aa	VLKDE D DP NDQNS .... LEHLDK VRN..... LIEK SKK		
1264sid2	<b>VLKDE D NS NDQSV .... LEHLDK VRN..... LIEK SOE</b>		
U37359aa	VLANHPD FN PD PKMTQAI QSFCEK E ENAERE.. ....R		
U58987aa	VLANHPN FN PD PKMTQAI QSFCEK E DSAERE.. ....R		
D11463aa	SLQDVPH RP ..HDK..DAT SKYL EQ E RDANEETK QKTA DGEGD		
X82322aa	LS V S PP MVENK..KEV LTYL SK E A TEANAQWY EA...QG V		

	401		450
AB010695aa	VNRSEIKLP LVRIKVDYSG .....F MTINPQREGQ KYVGKVANPQ		
AJ243822aa	VNRSEIKLP LVRIKVDYSG .....F MTINPQREGQ KYVGKVANPQ		
1264sid2	<b>ASRSEPKLP LVRIKVDYSG .....F STINPQREGQ KYVGKVANPQ</b>		
U37359aa	LGNSHQEKP LVR VDYSG .....GF EPFSVLRESQ K VD VANHK		
U58987aa	LGNPQOEKP L R VDYSG .....GF EPFNVLRESQ K VD VANHK		
D11463aa	MV...ELPK L R VDYSA PSNTQSPID QVENPRRES K VG VANG		
X82322aa	VVENKEPLP L R VDY G .....G QVENPQRES K VG VANAT		

	451		500
AB010695aa	DILIE....S K K KGR EA .N...IDDSE	LRE...EELN QONTEALV..	
AJ243822aa	DILIE....S K K KGR EA .N...IDDSE	LRE...EELN QONTEALV..	
1264sid2	DILIE....S K K KGR EA .N...IDDSE	LRE...EELN QONTEALV..	
U37359aa	DI H FRHRE Q..E T GEE INFGK....IT E.SE.GT TLR EDLVKQ		
U58987aa	D H FRHRE Q..E T GEE INFGM....IT EASE.GA TLR EDLVKQ		
D11463aa	N QFYKKRS PV S K E INGTSISR VE LFSSGG ELE Q LVND		
X82322aa	N QFYLKKK .Y S ARNDG LYTSA EDIK I.....N SLR E LVNE		

	501		550
AB010695aa	....AESNLK MEILPVDID	ALHNEVNKD DK AFYSC Q	YNIQETPGKI
AJ243822aa	....AESNLK MEILPVDID	ALHNEVNKD DK AFYSC Q	YNIQETPGKI
1264sid2	....AESNLK MEILPVDID	ALHNEVNKD DK AFYSC Q	YNIQETPGKI
U37359aa	YFQTAEKN Q S LTERG G EA Q EVDK KDAIEEL K Y LEKIQRFI		
U58987aa	YFQTAEKN Q S LTERG G EA Q EVDK KDAIEEL K Y LEKIQRFI		
D11463aa	LL....NK Q S L EGVGN EA KKEVDK K TALKEF S HEI SNEVGII		
X82322aa	YL....KTN ECLFEDSIG EA VNEVEKD D DAIKE~~~		

	551		600
AB010695aa	K DAKKE E D I KVGE C EER K RS	.....E.P	ICSS....
AJ243822aa	K DAKKE E D I KVGE C EER K RS	.....E.P	ICSS....
1264sid2	S DAKKE E D I KVGE C EER K RS	LHSK CIRT	ICSHNLVF
U37359aa	KERHID LE KIDEEV RFR ETRO NTNEE DDEVRE MTR R LRSQSEE		
U58987aa	KERHID LE KIDEEV RFR ESRQNTNEE DDEVRE MSR R LRSQSET		
D11463aa	S NEFL T A E KALIK Q KRANSVP TPPK NDET N FAFNGNGLDS		
X82322aa	~~~~~		

	601		650
AB010695aa	LSTG TSEN TKCS GIANA SFSDDEDTTQ	MSGLAPPTRG	RRGSSTANTT
AJ243822aa	LSTG TSEN TKCS GIANA SFSDDEDTTQ	MSGLAPPTRG	RRGSSTANTT
1264sid2	LSLN FSFC FPG CYWLA SNSYN	~~~~~	~~~~~
U37359aa	S SAFS DD MSIDLAEQMA NDSDDISAA	TNKGRRGRG	RRGGRQNSA
U58987aa	S SAFS ED .SFD SEQTA NDSDDSLSAV	PSRGRGRG	RRGARGQSSA
D11463aa	FRSSNREVRT GSPDITQSHV D NESR THIS	QAESSKPTSK	PKRVRTATKK
X82322aa	~~~~~		

	651		700
AB010695aa	RGRAKAPTRG RGRGKASSAM KQTTLDSSLG	FRQSQRSASA	AASAAFKSAS
AJ243822aa	RGRAKAPTRG RGRGKASSAM KQTTLDSSLG	FRQSQRSASA	AASAAFKSAS
1264sid2	~~~~~	~~~~~	~~~~~
U37359aa	SRGGSQRGR. ....	.....AFKS	TRQQPSRNV
U58987aa	PRGGSQRGRD TGLEITTRGR SSKATSSTSR	NMSIIDAFRS	TRQQPSRNV
D11463aa	KIPAFSDSTV ISDAENELGD NDAQDDVDI	DENDIIMVST	DEEDASYGLL
X82322aa	~~~~~		

	701		750
AB010695aa	TIGEDDVDSF SSEEVEPDF NKPDSSEDD	ESTKGKGRKR	PATTKRGRGR
AJ243822aa	TIGEDDVDSF SSEEVEPDF NKPDSSEDD	ESTKGKGRKR	PATTKRGRGR
1264sid2	~~~~~	~~~~~	~~~~~
U37359aa	TKNYSEVIEV DESDVEEDIF PTTSKTDQRW	SSTSSSKIMS	QSQVSKGVDF
U58987aa	PKNYSETIEV DSD.EDDIF PTNSRADQRW	SGTTSSKRMS	QSQTAKGVDF
D11463aa	NGRKTCTKTR PAASTKTASR RGKGRASRTP	KTDILGSLA	KKRK~~~~~
X82322aa	~~~~~		

	751				800
AB010695aa	GS	TSKRGRK	NESSSSLNRL	LSSKDDDEDE	DDEDREKKLN KSQPRVTRNY
AJ243822aa	GS	TSKRGRK	NESSSSLNRL	LSSKDDDEDE	DDEDREKKLN KSQPRVTRNY
<b>1264sid2</b>	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
U37359aa	ES	EDDDDDP	FMNTSSLRRN	RR~~~~~	~~~~~
U58987aa	ES	EDDDDDP	FMSSSCPRRN	RR~~~~~	~~~~~
D11463aa	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~
X82322aa	~~~~~	~~~~~	~~~~~	~~~~~	~~~~~

	801
AB010695aa	GALRR
AJ243822aa	GALRR
<b>1264sid2</b>	~~~~~
U37359aa	~~~~~
U58987aa	~~~~~
D11463aa	~~~~~
X82322aa	~~~~~



## Mre11\_DNA\_bind

Accession number: PF04152

Previous identifiers: Mre11\_DNA\_bind;

**Mre11 DNA-binding presumed domain**[Add/Annotation](#)

The Mre11 complex is a multi-subunit nuclease that is composed of Mre11, Rad50 and Nbs1/Xrs2, and is involved in checkpoint signalling and DNA replication [1]. Mre11 has an intrinsic DNA-binding activity that is stimulated by Rad50 on its own or in combination with Nbs1 [2].

**INTERPRO description (entry IPR007281)**

The Mre11 complex is a multi-subunit nuclease that is composed of Mre11, Rad50 and Nbs1/Xrs2, and is involved in checkpoint signalling and DNA replication MEDLINE:11988766. Mre11 has an intrinsic DNA-binding activity that is stimulated by Rad50 on its own or in combination with Nbs1 MEDLINE:10823903.

**QuickGO****FUNCTION :** manganese ion binding (GO:0030145)**PROCESS :** double-strand break repair (GO:0006302)**COMPONENT :** nucleus (GO:0005634)**Alignment**☒ Seed (10) ☐ Full (31)Format **Coloured alignment**[Get alignment](#)[View HMM logo](#)

[Further alignment options here](#)  
[Help relating to Pfam alignments here](#)

**Species Distribution****Domain organisation**

- ☒ View 1 representative architecture  
☐ View architectures for 31 proteins

Zoom  pixels/aa.[View Graphic](#)**Phylogenetic tree**



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<b>NEW!</b> View alignments & domain organisation by species					<input checked="" type="radio"/> Seed (10) <input type="radio"/> Full (31)
Tree depth : <a href="#">Show all levels</a>					<a href="#">Download tree</a>
<a href="#">View Species Tree</a>					<a href="#">ATV Applet</a>
The trees were generated using <a href="#">Quicktree</a> To find out more about ATV phylogenetic tree-viewer <a href="#">click here</a>					

### Database References

<b>SYSTERS</b>	<a href="#">Mre11_DNA_bind</a>
<b>PANDIT</b>	<a href="#">Mre11_DNA_bind</a>
<b>FUNSHIFT</b>	<a href="#">Mre11_DNA_bind</a>

### Literature References

**1.**  
**A mechanistic basis for Mre11-directed DNA joining at microhomologies.**

Pauli TT, Gellert M;  
 Proc Natl Acad Sci U S A 2000;97:6409-6414.

**2.**  
**The Mre11 complex: at the crossroads of dna repair and checkpoint signalling.**

D'Amours D, Jackson SP;  
 Nat Rev Mol Cell Biol 2002;3:317-327.

### Pfam specific information

Author of entry	Wood V, Finn RD
Type definition	Domain
Source of seed members	Pfam-B_3909 (release 7.3);
Average Length	201.4
Average %id	37
Average Coverage	28.62%

### HMMER build information

	<b>Pfam_ls [Download HMM]</b>	<b>Pfam_fs [Download HMM]</b>
Gathering cutoff	25.0 25.0;	25.0 25.0
Trusted cutoff	71.9 71.9;	49.5 32.0
Noise cutoff	13.1 13.1;	8.2 17.4
Build method of HMM	hmmbuild -F HMM_ls SEED hmmcalibrate --seed 0 HMM_ls	hmmbuild -f -F HMM_fs SEED hmmcalibrate --seed 0 HMM_fs

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## Metallophos



**Figure 1: 1hpu Hydrolase**

5-nucleotidase (closed form), complex with ampcp

**Key:**

Domain	Chain	Start Residue	End Residue
Metallophos	A	34	256
5 nucleotid C	A	363	511
Metallophos	B	34	256
5 nucleotid C	B	363	511
Metallophos	C	34	256
5 nucleotid C	C	363	511
Metallophos	D	34	256
5 nucleotid C	D	363	511

The Swissprot/PDB mapping was provided by MSD

1aui

Display pdb

Accession number: PF00149

Previous identifiers: STphosphatase;

**Calcineurin-like phosphoesterase**[Add Annotation](#)

This family includes a diverse range of phosphoesterases [1], including protein phosphoserine phosphatases, nucleotidases, sphingomyelin phosphodiesterases and 2'-3' cAMP phosphodiesterases as well as nucleases such as bacterial SbcD [SBCD\\_ECOLI](#) or yeast MRE11 [MR11\\_YEAST](#). The most conserved regions in this superfamily centre around the metal chelating residues.

**RE!** This family forms **interactions** with other Pfam families, to view them click [here](#)

**INTERPRO description (entry IPR004843)**

Protein phosphorylation plays a central role in the regulation of cell functions [MEDLINE:2827745](#), causing the activation or inhibition of many enzymes involved in various biochemical pathways [MEDLINE:2176161](#). Kinases and phosphatases are the enzymes responsible for this, and may themselves be subject to control through the action of hormones and growth factors [MEDLINE:2827745](#). Serine/threonine (S/T) phosphatases catalyse the dephosphorylation of phosphoserine and phosphothreonine residues. In mammalian tissues four different types of PP have been identified and are known as PP1, PP2A, PP2B and PP2C. Except for PP2C, these enzymes are evolutionary related. The catalytic regions of the proteins are well conserved and have a slow mutation rate, suggesting that major changes in these regions are highly detrimental [MEDLINE:2827745](#).

The metallo-phosphoesterase motif is found in a large number of proteins involved in phosphorylation. These include serine/threonine phosphatases, DNA polymerase, exonucleases, and other phosphatases.

**QuickGO****FUNCTION :**hydrolase activity ([GO:0016787](#))**Alignment****Domain organisation**

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 ☐ Full (2362)

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**Species Distribution**

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**Phylogenetic tree**

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**Database References**

PDB  
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1g5b A; 13; 190;

PDB 2 Pfam  
 Scop|Cath|Pfam  
 Rasmol Chime Jmol  
 PDBSUM SCOP-UK MSD

**COGS**

COG0420 COG0622 COG0639 COG0737 COG1311 COG1407 COG1408 COG1409  
 COG1692 COG1768 COG2129 COG2908

**HOMSTRAD**

stpp

**PFAMB**

PB138897 PB138852 PB138821 PB138819 PB138082 PB137993 PB137778  
 PB137151 PB136893 PB136624 PB136447 PB136110 PB135893 PB135664  
 PB135104 PB134487 PB134107 PB133997 PB133801 PB133587 PB129622  
 PB121941 PB109640 PB095241 PB075242 PB065007 PB061303 PB051159  
 PB047522 PB046470 PB029770 PB022149 PB012730 PB001928

**SYSTERS**

Metallophos

**PANDIT**

Metallophos

**FUNSHIFT**

Metallophos

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Literature References							
1. <b>Phosphoesterase domains associated with DNA polymerases of diverse origins.</b> Aravind L, Koonin EV; Nucleic Acids Res 1998;26:3746-3752.						Author of entry	Dlatic M
						Type definition	Domain
						Source of seed member s	Dlatic M
						Average Length	195.5
						Average %id	15
						Average Coverage	50.41%

HMMER build information		
	Pfam_ls [ <a href="#">Download HMM</a> ]	Pfam_fs [ <a href="#">Download HMM</a> ]
Gathering cutoff	22.0 22.0;	14.0 14.0
Trusted cutoff	22.2 22.2;	14.0 14.0
Noise cutoff	21.9 21.9;	13.9 13.9
Build method of HMM	hmmbuild -F HMM_ls SEED hmmcalibrate --seed 0 HMM_ls	hmmbuild -f -F HMM_fs SEED hmmcalibrate --seed 0 HMM_fs

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**Replication**
**PDB Id**
**1ii7**

**Contents**
**Description**

- ☐ Header details
- ☐ Header records

**Protein chains**

- ☐ **A B** 333 a.a. \*

**Ligands**

- ☐ PO4
- ☐ SO4 ×3
- ☐ 101

**Metal ions**

- ☐ **MN** ×4

**Waters** × 264

\* Residue conservation analysis

**PDB Id:** 1ii7

**Name:** Replication

**Title:** Crystal structure of p. Furiosus mre11 with manganese and damp

**Structure:** Mre11 nuclease. Chain: a, b. Engineered: yes

**Source:** Pyrococcus furiosus. Archaea. Expressed in: escherichia coli.

**UniProt:** Q8U1N9 (Q8U1N9) [Pfam]

**Function:** (see GO annotation below)

**Resolution:** 2.20Å

**R-factor:** 0.222

**R-free:** 0.264

**Authors:** K.-P.Hopfner, A.Karcher, L.Craig, T.T.Woo, J.P. Carney, J.A.Tainer

**Date:** 20-Apr-01

**Related entries:** 1ii8

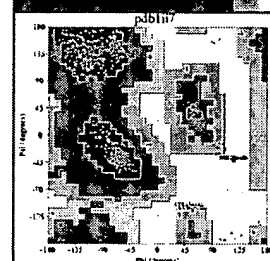
1f2t

1f2u


**Gene Ontology (GO) functional annotation**

Biological process	DNA metabolism	2 term (s)
		5 term (s)
Biochemical function	hydrolase activity	2 term (s)

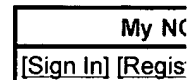
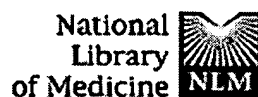
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1: Cell. 2001 May 18;105(4):473-85.

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**Cell Press**

Structural biochemistry and interaction architecture of the DNA double-strand break repair Mre11 nuclease and Rad50-ATPase

Hopfner KP, Karcher A, Craig L, Woo TT, Carney JP, Tainer JA.

Department of Molecular Biology and Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA 92037, USA.

To clarify functions of the Mre11/Rad50 (MR) complex in DNA double-strand break repair, we report *Pyrococcus furiosus* Mre11 crystal structures, revealing a protein phosphatase-like, dimanganese binding domain capped by a unique domain controlling active site access. The structures unify Mre11's multiple nuclease activities in a single endo/exonuclease mechanism and reveal eukaryotic macromolecular interaction sites by mapping human and yeast Mre11 mutations. Furthermore, the structure of the *P. furiosus* Rad50 ABC-ATPase with adjacent coiled-coil defines a compact Mre11/Rad50-ATPase complex and suggests that Rad50-ATP-driven conformational switching directly controls the Mre11 exonuclease. Electron microscopy, small angle X-ray scattering, and ultracentrifugation data of human and *P. furiosus* MR

reveal a dual functional complex consisting of a (Mre11)<sub>2</sub>/(Rad50)<sub>2</sub>  
heterotetrameric DNA processing head and a double coiled-coil linker

PMID: 11371344 [PubMed - indexed for MEDLINE]

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